

REMARKS

Claims 1 to 10 and 22 are under consideration
Claims 11 to 21 and 23 stand withdrawn from consideration.
New claim 24 is introduced. Claim 24 is based on the language
of claims 4 and 6.

The Office action refers to Election/Restrictions.

Applicant's election with traverse of the Group I (claims 1-10) in the reply filed on 11/28/2005 is acknowledged. The traversal is on the ground(s) that claims belong to the same class and should be examined together and there is no serious burden in searching and examining all groups of claims. This is not found persuasive because different groups of claims are drawn to products and methods having different scope as claimed and, thus, the references that would be applied to one group of claims would not necessarily anticipate or render obvious the other group(s). Moreover, as to the question of burden of search, classification of subject matter is also an indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. Clearly different searches and issues are involved with each group. For these reasons, the restriction requirement is deemed proper and is adhered to. The restriction requirement is hereby made FINAL.

Upon applicants' request claim 22 is rejoined with the Group I claims 1-10. However, instant claims 19-21 appear to provide for the use

of apparatus that belongs to non-elected invention(s). Moreover, the instant claims 19-21 do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. Thus, arguments with respect to claims 19-21 are moot.

Claims 11-21 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 11/28/2005.

Applicant respectfully asks to defer any response to the Restriction Requirement until a Final action is issued in this case.

Claims 1-10 and 22 are under examination in the instant office action.

The Office Action refers to Claim Objections.

Claims 1-22 stand objected to because of the following informalities:

Claim 3 does not indicate dependency as intended. Claims 4-6, 9 are objected to under 37 UR 1.75(c) as being in improper form. See MPEP § 608.01(n). Appropriate corrections are required.

The present amendment makes claim 3 dependent on claim 1. According to the present amendment, claim 9 will depend only on claim 4.

The Office Action refers to Claim Rejections - 35 USC § 102.

1. Claims 1-5, 7-10 and 22 stand rejected under 35 U.S.C. 102(b) as being anticipated by US 4,857,464 (Weathers et al) (IDS reference). Claims are directed to a method for cultivation cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semi permeably separated from the supply container; step feeding cells with gas/cell cultivation medium mixtures; step obtaining products. Some Claims are further drawn to the cells being plant or mammalian cells. Some Claims are further drawn to gas/cell cultivation medium mixtures such as mist with droplets up to 5000 micrometers. Some claims are further drawn to feeding by spray generated by ultrasound.

US 4,857,464 (Weathers et al) teaches a method for cultivation cells and obtaining the products from these cells in a mist cultivation reactor wherein the method comprises step of culturing cells in cultivation chamber(s) that semi permeably separated from the supply container with mesh and/or membrane (devices 301 and 302 an Fig. 4 and devices 14 and 33 an Fig. 5) and step of feeding cells with gas/cell cultivation medium mixtures in a form of mist having droplets up to 5000 micrometres (col. 2, lines 45050) and generated by ultrasound devices (col. 3, lines 1-10). The cells include plant cells and animal cells including mammalian hydrodomas (table 1; col. 2, line 69; col.5, line 33) that are cultured at high densities or at high yields (col. 5, line 15). The products are dissolved in the feeding mixture and collected below the cultivation chambers. Thus, the cited reference teaches identical steps and structural

elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

The rejection is respectfully traversed.

The reference Weathers et al. in United States Patent 4,857,464 teaches that animal cells can be raised at a rolled together grid, which has a large surface, compare column 2, lines 63 to 68:

“Coalesced nutrient drains through the support to be collected within a sump area for retrieval of products and reuseable media. In another embodiment, a convoluted mesh of biological inert material provides a large surface area upon which attaching organisms, such as animal cells may grow.”

The basic problem in connection with the cultivation of animal cells of high density is the oxygen supply of the cells, which are not located at the surface. Therefore Weathers teaches to employ a large surface for the cultivation of animal cells. However, the reference Weathers does not reach high densities, as compared to the high densities obtained according to the present invention. “High yields” in column 5, line 15 of the reference Weathers et al. does not mean “high density”. For this reason the fog reactors according to the Weathers et al. reference (USP 4,857,464) have up to now not been

employed for a cultivation of animal cells. The problem of oxygen supply does not arise in connection with plant cells. A further disadvantage of the teaching of the reference Weathers comprises that a rolled together grid would not be in a position to hold back the cells. The cells would have to be immobilized. No high densities would be possible with immobilization. The pillow like device of Weathers et al. , column 5, line 5 and also Fig. 5 would not be in a position to hold back the cells.

2. Claims 1-4, 7, 9, 10 and 22 stand rejected under 35 U.S.C. 102(b) as being anticipated by US 6,255,106 (Marx et al). Claims are directed to a method for cultivation cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semi permeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the cells being mammalian cells. Some claims are further drawn to the use of semi permeable membrane for Separation. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid.

US 6,255,106 (Marx et al) teaches a method for cultivation mammalian cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) semi permeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures and step obtaining product (Fig. 1; col. 1, lines 56-65; col. 2, lines 28-30 and lines 52). Thus, the cited reference teaches

identical steps and structural elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

Applicant respectfully disagrees. The reference Marx et al. does not teach to cultivate animal cells in high density. The term "high density" does not appear a single time in the reference Marx et al. . Also in addition it would not have been possible to cultivate animal cells in high density with the method of Marx et al. The oxygen supply to the animal cells would be insufficient even though the cells are disposed in membranes. The reason for the insufficiency is that not enough oxygen can be disposed in the liquid phase of the cell culturing face.

3. Claims 1-7, 9, 10 and 22 stand rejected under 35 U.S.C. 102(b) as being anticipated by Knazek(Federation Proceedings. 1974. Vol.33, NO. 8, pages 1978-1981).

Claims are directed to a method for cultivation cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the cells being mammalian cells. Some claims are further drawn to the use of semipermeable membrane for separation and to membrane made from polycarbonate. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid.

The reference by Knazek discloses a method for cultivation mammalian cells at high densities for obtaining the secretion products from these cells wherein the method comprises step of culturing cells in polycarbonate capillaries or in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures (fig. 2) and step obtaining secretion products, for example: prolactin (see fig. 2). Thus, the cited reference teaches identical steps and structural elements as required by the claimed method. Therefore, the cited reference is considered to anticipate the claimed invention.

Applicant respectfully traverses.

The reference Knazek et al. in fact describes a stationary cultivation at high cell densities, however a uniform supply with nutrients and in particular the oxygen supply is questionable with the Knazek et al. reference.

The Office Action refers to Claim Rejections - 35 USC § 103.

Claims 1-10 and 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,857,464 (Weathers et al), US 6,255,106 (Marx et al) and Knazek (Federation Proceedings. 1974. Vol.33, NO. 8, pages 1978-1981). Claims are directed to a method for cultivation cells at high densities for obtaining the products from these cells wherein the method comprises step of culturing cells in cultivation chamber(s) that semipermeably separated from the supply container, step of feeding cells with gas/cell cultivation medium mixtures, step obtaining product. Some claims are further drawn to the cells being plant or mammalian cells. Some claims are further drawn to the use of semipermeable membrane

for Separation and to membrane made from polycarbonate. Some claims are further drawn to gas/cell cultivation medium mixtures such as bubbles in liquid or in a form of mist having droplets up to 5000 micrometres. Some claims are further drawn to feeding by spray generated by ultrasound. The cited US 4,857,464 (Weathers et al), US 6,255,106 (Marx et al) and Knazek are relied upon as explained above for the disclosure of culturing cells including plant cells and mammalian cells at high densities for obtaining the products from these cells. The semipermeable membranes used for separation of cultivation chambers from supply container in all cited methods and the membrane materials include polycarbonate (Knazek). The feeding of cells is provided by gas/cell cultivation medium mixtures in all cited methods including the use of mist having droplets up to 5000 micrometres (US 4,857,464).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify membrane materials and form of gas/liquid feeding mixtures with a reasonable expectation of success in culturing cells including plant cells and mammalian cells at high densities for obtaining the products from these cells as adequately demonstrated by the cited references. It would be within the purview of ordinary skill in the art to adjust form of gas/liquid feeding mixtures with regard to the cells used for production of desired products and to choose membrane materials that are available and known for culturing cells. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.


Applicants respectfully disagree.

Neither Weathers et al, Marx et al. nor Knazek et al. resolve the problem of oxygen supply of animal cells in a sufficient manner. It is therefore completely unexpected that a satisfactory oxygen supply can be established for animal cells and at the same time the cultivation of cells in high density is made possible by way of membranes and a gas/media mixture, wherein the animal cells are still sufficiently supplied with nutrients.

Reconsideration of all outstanding rejections is respectfully requested.

All claims as presently submitted are deemed to be in allowable form.

Respectfully submitted,
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